UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,310	11/21/2003	Paul G. Brunetta	P1979R1	3292

9157 7590 11/30/2007

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
11/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,310	BRUNETTA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3, 8-14 and 16 are pending.

2. The following new grounds of rejections are necessitated by the amendment filed 9/18/07.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-3, 8-14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over newly cited US Pat No. 5,525,625 (issued June 1996; PTO 892) in view of WO 98/02540 (of record, January 22, 1998; PTO 1449) and WO 01/15730 publication (of record, March 8, 2001; PTO 1449).

The '625 patent teaches a method of treating proliferative disorder such as psoriasis and cancer by administering a MAP kinase inhibitor such as 2-(2amino-3-methoxyphenyl)-4-oxo-4H[1]benzopyran (see entire document, col. 3, lines 60-67, claims of the '625 patent, in particular).

The invention differs from the teachings of the reference only in that the method of therapeutic treatment psoriasis is an antibody that binds to ErbB2 and blocks ErbB2 signaling through the MAP kinase pathway.

The WO 98/02540 publication teaches ErbB2 plays a role in psoriasis and a method of treating psoriasis by administering to the mammal with an agent that blocks the ErbB2 ligand from binding to its receptor ErbB2 such as soluble ErbB2 receptor that comprises extracellular domain of ErbB2 fused to IgG (see page 35, line 11, homodimer, abstract, in particular). The WO 98/02540 publication teaches blocking ErbB2 using ErbB antagonist such as ErbB2 and ErbB3 or ErbB2 and ErbB4 fused to Fc prevents the ErbB ligand from binding and activation of the ErbB receptor (see page 25, lines 1-10, page 23, lines 23-31, heterodimer, abstract, claims 37-40, in particular).

The WO 01/15730 publication teaches a method of treating a benign hyperproliferative epithelial, inflammatory angiogenic immunological disorders (see page 14, lines 9-14, page 30, lines 31-38, in particular) by administering to a mammal such as human, dogs, horses, (see abstract, page 14, lines 4-8, in particular) an effective amount of an antibody which binds ErbB2 such as humanized version of 4D5 also known as HERCEPTIN®, 7C2, 7F3, 4D5, 2C4 (see page 33, in particular). The reference monoclonal antibodies such as 7C2, 7F3, 4D5 obviously block the ErbB2 ligand from activating its receptor, ErbB2. The reference humanized version of the antibody 2C4 obviously competes with the monoclonal antibody 2C4 because it contains the same CDRs as the mouse monoclonal antibody 2C4 and binds to the same epitope. The WO 01/15730 publication further teaches the humanized form of 2C4 (see page 5, lines 34, in particular) and antibody fragment thereof such as Fab or Fv (see page 11, lines 26-37, page 12-13, in particular). The reference antibody is not conjugated to with a cytotoxic agent (see page 33, page 14, lines 30-33, claim 1 of WO 01/15730 publication, in particular). The WO 01/15730 publication teaches administering to the patient such as human a second therapeutic agent such as chemotherapeutic agent (see page 14, lines 34-38 through page 15, lines 1-29, in particular), a growth inhibitory agent (see page 15, lines 30 through page 16, lines 1-2, in particular), or anti-ErbB2 or binding fragment thereof conjugated to a cytotoxic agent such as bacterial toxin (see page 25, lines 31-39, page 26, lines 1-11, in particular). The reference antibody is administered at least one dose to the patient in an amount from about 4mg/kg and not exceeding 30mg/kg, which is within the claimed limitation of about 0.5mg/kg to about 30 mg/kg.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat psoriasis by substituting the MAP kinase inhibitor 2-(2amino-3-methoxyphenyl)-4-oxo-4H[1]benzopyran of the '625 patent or the ErbB2-IgG immunoadhesin that blocks ErbB2 ligand from binding to ErbB2 as taught by the WO 98/02540 publication for the antibody or binding fragment thereof that binds to ErbB2 and thereby preventing the binding

of ErbB2 ligand to its receptor as taught by the WO 01/15730 publication wherein the reference antibody can be conjugated to a cytotoxic agent or not conjugated to a cytotoxic agent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '625 patent teaches MAP tyrosine kinase inhibitor is useful for treating psoriasis, see claims of the '625 patent. The WO 98/02540 publication teaches blocking ErbB2 ligand from binding to ErbB2 receptor is useful for treating psoriasis (see page 35, line 11, homodimer, abstract, in particular). The WO 01/15730 publication teaches antibody that binds specifically to ErbB2 is useful for treating hyperproliferative epithelial, inflammatory and angiogenic immunological disorders (see page 14, lines 9-14, page 30, lines 31-38, in particular).

Applicants' arguments filed 9/18/07 have been fully considered but are not found persuasive.

Applicants' position is that there is nothing that would make a person skilled in the art select psoriasis out of the numerous diseases and conditions listed in WO98/02540 than the teaching of the present invention. The skilled artisan would be required to select the once mentioned psoriasis of the long list of diseases targeted by the heteromultimer adhesions of WO98/02540 and must assume that the anti-ErbB2 antibodies of the WO01/157030 will behave of the same way as the ErbB heteromultimer adhesions of the WO 98/02540. There is no reasonable expectation that the antibodies of the present invention would be effective in the treatment of psoriasis. As explained in the previous response to the previous Office action, psoriasis is a chronic diseases that is difficult to treat. A reasonable expectation that such treatment is likely to work by following the methods of the present invention has only been created by demonstrating the ability of the antibodies herein to block signaling through MAP kinase pathway, this feature is now recited in the claims.

Contrary to applicant's argument that there is no expectation of success in treating psoriasis by blocking signaling through MAP kinase pathway, the use of tyrosine kinase inhibitor to block MAP kinase pathway for treatment of psoriasis is known in the art as evidenced by the teachings of the US Pat No. 5,525,625 (see entire document, col. 3, lines 60-67, claims of the '625 patent, in particular). With respect to the argument that the present invention has only been created by demonstrating the ability of the antibodies herein to block signaling through MAP kinase pathway, it is noted that the specification discloses blocking of MAP kinase pathway using

anti-ErbB2 in breast cancer cell line MCF7 cells; these breast cancer cells are not even the right cell types (model) to be responsible for the chronic psoriasis, see example 4, paragraph 0282. Further, there is no evidence in the specification as filed that any patient with psoriasis has been treated with anti-ErbB2 antibody such as rhuMab 2C4 or humanized 7F3 antibody.

6. Claims 1-3, 8-14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over the newly cited US Pat No. 5,525,625 (issued June 1996; PTO 892) in view of US Pat 5,650,415 (of record, issued July 22, 1997; PTO 892) and WO 01/15730 publication (of record, March 8, 2001; PTO 1449).

The '625 patent teaches a method of treating proliferative disorder such as psoriasis and cancer by administering a MAP kinase inhibitor such as 2-(2amino-3-methoxyphenyl)-4-oxo-4H[1]benzopyran (see entire document, col. 3, lines 60-67, claims of the '625 patent, in particular).

The claimed invention differs from the teachings of the reference only in that the method for therapeutic treatment of psoriasis by administering to the human a therapeutic effective antibody which binds to ErbB2 instead of tyrokine kinsae inhibitor that block MAP kinase pathway.

The '415 patent teaches that tyrosine kinase includes HER family such as EGFR, HER2, HER3 and HER4, and many of these kinases have been found to be involved in cellular signaling pathways leading to pathogenic conditions such as cancer, psoriasis, and hyperimmune response, etc (see col. 1, lines 24-41, in particular). The '415 patent teaches that various tyrosine kinase inhibitors such as the compounds as shown in the Summary of the Invention are useful for treating various cell proliferative disorders involving HER2 such as cancers and psoriasis (see summary of invention, claims 2-3 and 8 of the '415 patent, in particular). The '415 patent further teaches compounds show to have good effect against HER2 are likely to also have good effect against other members of the Her family (see col. 3, line 18-32, col. 4, lines 40-45, in particular).

The WO 01/15730 publication teaches a method of treating a benign hyperproliferative epithelial, inflammatory angiogenic immunological disorders (see page 14, lines 9-14, page 30, lines 31-38, in particular) by administering to a mammal such as human (see abstract, page 14, lines 4-8, in particular) an effective amount of an antibody which binds ErbB2 such as humanized version of 4D5 also known as HERCEPTIN®, 7C2, 7F3, 4D5, 2C4 (see page 33, in particular). The reference monoclonal antibodies such as 7C2, 7F3, 4D5 obviously block the ErbB2 ligand from activating the ErbB2 receptor because these antibodies bind to the extracellular domain of

ErbB2. The WO 01/15730 publication further teaches the humanized form of 2C4 (see page 5, lines 34, in particular) and antibody fragment thereof such as Fab or Fv (see page 11, lines 26-37, page 12-13, in particular). The reference humanized version of the antibody 2C4 or Fab fragment inherently competes with the monoclonal antibody 2C4 because it contains the same CDRs as the mouse monoclonal antibody 2C4 and binds to the same epitope as monoclonal antibody 2C4. The reference antibody is not conjugated to with a cytotoxic agent (see page 33, page 14, lines 30-33, claim 1 of WO 01/15730 publication, in particular). The WO 01/15730 publication teaches administering to the patient such as human a second therapeutic agent such as chemotherapeutic agent (see page 14, lines 34-38 through page 15, lines 1-29, in particular), a growth inhibitory agent (see page 15, lines 30 through page 16, lines 1-2, in particular), or anti-ErbB2 or binding fragment thereof conjugated to a cytotoxic agent such as bacterial toxin (see page 25, lines 31-39, page 26, lines 1-11, in particular). The reference antibody is administered at least one dose to the patient in an amount from about 4mg/kg and not exceeding 30mg/kg, which is within the claimed limitation of about 0.5mg/kg to about 30 mg/kg.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat psoriasis by blocking ErbB2 signaling through the MAP kinase pathway by substituting the MAP kinase inhibitor 2-(2amino-3-methoxyphenyl)-4-oxo-4H[1]benzopyran of the '625 patent or the various tyrosine kinase inhibitor such the compounds as shown in the Summary of the Invention that blocks ErbB2 signaling for treating psoriasis of the '415 patent for the antibody or binding fragment thereof which binds to ErbB2 that is useful for treating benign hyperproliferative epithelial, inflammatory angiogenic immunological disorders as taught by the WO 01/15730 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated with the expectation of success in treating posoriasis by blocking ErbB2 signaling through MAP kinase pathway because the '625 patent teaches administering a MAP kinase inhibitor such as 2-(2amino-3-methoxyphenyl)-4-oxo-4H[1]benzopyran is useful for treating proliferative disorder such as psoriasis and cancer (see entire document, col. 3, lines 60-67, claims of the '625 patent, in particular). The '415 patent teaches that various tyrosine kinase inhibitors such as the compounds as shown in the Summary of the Invention are useful for treating various cell proliferative disorders involving HER2 such as cancers and psoriasis (see summary of invention, claims 2-3 and 8 of the '415 patent, in particular). The WO 01/15730 publication teaches antibody which

binds to ErbB2 alone or conjugated antibody that binds to ErbB2 is useful for treating a benign hyperproliferative epithelial, inflammatory angiogenic immunological disorders (see page 14, lines 9-14, page 30, lines 31-38, in particular).

Applicants' arguments filed 9/18/07 have been fully considered but are not found persuasive.

Applicants' position is that there is nothing that would make a person skilled in the art select psoriasis out of the numerous diseases and conditions listed in WO98/02540 than the teaching of the present invention. The skilled artisan would be required to select the once mentioned psoriasis of the long list of diseases targeted by the heteromultimer adhesions of WO98/02540 and must assume that the anti-ErbB2 antibodies of the WO01/157030 will behave of the same way as the ErbB heteromultimer adhesions of the WO 98/02540. There is no reasonable expectation that the antibodies of the present invention would be effective in the treatment of psoriasis. As explained in the previous response to the previous Office action, psoriasis is a chronic diseases that is difficult to treat. A reasonable expectation that such treatment is likely to work by following the methods of the present invention has only been created by demonstrating the ability of the antibodies herein to block signaling through MAP kinase pathway, this feature is now recited in the claims.

Contrary to applicant's argument that there is no expectation of success in treating psoriasis by blocking signaling through MAP kinase pathway, the use of tyrosine kinase inhibitor to block MAP kinase pathway for treatment of psoriasis is known in the art as evidenced by the teachings of the US Pat No. 5,525,625 (see entire document, col. 3, lines 60-67, claims of the '625 patent, in particular). With respect to the argument that the present invention has only been created by demonstrating the ability of the antibodies herein to block signaling through MAP kinase pathway, it is noted that the specification discloses blocking of MAP kinase pathway using anti-ErbB2 in breast cancer cell line MCF7 cells; these breast cancer cells are not even the right cell types (model) to be responsible for the chronic psoriasis, see example 4, paragraph 0282. Further, there is no evidence in the specification as filed that any patient with psoriasis has been treated with anti-ErbB2 antibody such as rhuMab 2C4 or humanized 7F3 antibody.

7. No claim is allowed.

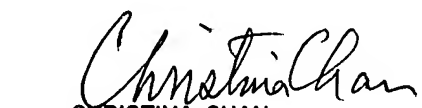
8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

10. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
November 23, 2007



CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600